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TITLE: Combined Use of Tissue Morphology, Neural Network Analysis of Chromatin Texture & Clinical Variables to Predict Prostate Cancer Agressiveness From Biopsy Mater

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13. ABSTRACT *(Maximum 200 Words)*

Purpose: To combine clinical, serum, pathologic and computer derived information into an artificial neural network to develop/validate a model to predict prostate cancer tumor aggressiveness in both a retrospective and prospective cohort of men with clinically localized prostate cancer both prior to and after radical prostatectomy.
Scope: Prospective enrollment of 500 men who are scheduled to undergo radical retropubic prostatectomy (year 01). Development of an artificial neural network (year 02). Prospective validation of this model (projected year 03). All models will be tested and developed for biopsy and prostatectomy material.
Major Findings: To date, we have completed prospective enrollment of 557 men, collected tissue, serum and clinical/pathological information for 493 and completed computer image data analysis of 402 samples. We currently have begun construction of a model to predict prostate cancer aggressiveness and anticipate completion of this task by December 2000. At this time, prospective enrollment of a validation subset will begin.

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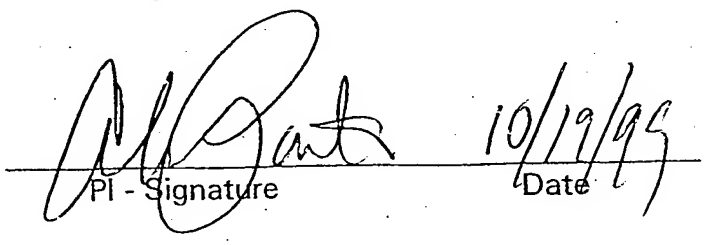

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October 30, 2000

Department of the Army
US Army Medical Research and Materiel Command
ATTN.: MCMR-RMI-S
504 Scott Street
Fort Detrick, MD 21702-5012

Dear Ms. Judy Pawlus,

Please find enclosed our annual summary for our project entitled *Combined Use of Tissue Morphology, Neural Network Analysis of Chromatin Texture and Clinical Variables to Predict Prostate Cancer Aggressiveness from Biopsy Material.* The summary details a description of the training for the project and a list of research accomplishments to date.

The information contained within this report does not contain any proprietary/or unpublished information. Therefore, no pages are marked for protection.

Please do not hesitate to contact me if you have any questions or concerns regarding any information contained within.

Sincerely,

Leslie Mangold

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Johns Hopkins University
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Enclosure

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Introduction:

Several specific objectives were outlined for our research proposal entitled *Combined use of Tissue Morphology, Neural Network Analysis of Chromatin Texture and Clinical variables to Predict Prostate Cancer Aggressiveness from biopsy Material.* We proposed to combine standard prognostic methods (clinical stage, PSA, Gleason score, and biopsy information) with Neural Network analysis of chromatin texture and computer derived tissue morphology prospectively to predict pathologic stage. We also intended to retrospectively investigate in prostatectomy specimens using a similar combination of clinical, histologic and computer derived characteristics to predict disease recurrence following surgery. This resulting technology and nuclear analysis would then be applied to study a group of men with long term follow-up after surgery to develop and validate this technology in predicting recurrence following surgery. Lastly, we intended to use this methodology to develop and validate an accurate model for predicting time to metastatic progression/death after biochemical recurrence. With these specific objectives outlined, a statement of work was submitted detailing the task and time line necessary to accomplish the goals of the proposal. Task one of our statement of work outlined the steps involved in the prospective enrollment of 500 men for prediction of pathologic stage model development. Completion of this objective was projected for 9 months following the initiation of this project. Below are the initial steps outlined in Task one, followed by an update of our progress to date.

Body: Specific aims

A. Identification and prospective enrollment of consecutive radical prostatectomy cases performed at the Johns Hopkins Hospital.

557 patients have been enrolled with 409 successfully fulfilling all inclusion criteria. The exclusion of 148 patients was due to: canceled RRP, no response from original biopsy institution, no cancer present in remaining biopsy material.

B. Obtain tissue blocks for each case.

Tissue blocks have been obtained for all patients admitted into this research study.

C. Cut and prepare histologic sections.

Histologic sections have been obtained from all cases.

6

D. Measure nuclear features with the QNG model.

Image analysis has been completed on 402 (98%) cases.

E. Enter all clinical, pathological, and quantitative nuclear data into the computer.

Clinical and pathological data for 409 patients has been collected and organized into a relational database.

F. Multivariate analysis to determine optimal prognosis prediction model.

DNA ploidy analysis and pathologic review has been completed on 402 cases (98%). Model construction has begun and should be complete by December 2000.

Task two of our approved statement of work details the steps necessary for prospective enrollment of 400 men for pathologic stage model validation. This portion of the project has a projected completion of 13 months following project initiation.

The initiation of this task has been delayed until model construction and image analysis is completed.

Task three of the research proposal outlines the steps involved in predicting tumor aggressiveness from biopsy/prostatectomy specimens. This portion of the statement of work should be completed by month 14 of the study. Our progress to date is indicated below:

A. Obtain tissue blocks from 300 cases treated at Johns Hopkins with radical prostatectomy.

300 pathological specimens have been identified. Collection of these cases has begun and should be complete by January 2001.

B. Cut histologic sections and prepare slides for QNG analysis.

This portion of task three will be conducted following completion of section A with an anticipated date of completion of April 2001

C. QNG determinations

Refer to task 3, section B comment.

D. Tissue morphology analysis.

Refer to task 3, section B comment.

F. Enter clinical data, pathological information, QNG results and tissue morphology into a database.

Clinical and pathological data for 300 patients has been collected and organized into a relational database.

G. Calculate model for prediction of post-operative progression from prostatectomy specimens.

This step will be completed following collection of all data involved with task three. Anticipated completion of this initiative May 2001.

Task four involves validation analyses from prostatectomy specimens for prediction of tumor aggressiveness. Our initial statement of work projected completion of this portion of the project by month 30 (March 2001). The identification and analysis of these additional 100 prostatectomy specimens will begin immediately following the tumor aggressiveness model construction detailed in task three. We believe that completion of this initiative will be prior to month 30 deadline initially proposed.

Lastly, task five of this research study involves retrospective development of a model for prediction of development of metastasises/death following biochemical recurrence following surgery. This task involves identification of 300 men who have exhibited biochemical or metastatic recurrence following surgery.

A. Obtain tissue blocks from 300 cases treated at Johns Hopkins with radical prostatectomy.

Tissue blocks for 304 cases have been collected.

B. Cut histologic sections and prepare slides for QNG analysis.

Histologic sections have been obtained for all cases identified for this task.

C. QNG determinations

Feulgan staining has been completed on 100 (33%) cases. Pathologic review has begun on these cases. QNG analysis will proceed following pathologic review of the stained slides.

D. Tissue morphology analysis.

Tissue morphologic analysis will proceed following pathologic review of the Feulgan stained slides.

F. Enter clinical data, pathological information, QNG results and tissue morphology into a database.

Clinical and pathological data for 304 patients has been collected and organized into a relational database.

G. Determine the prognostic significance of combined variables to predict 3, 5 and 7 year likelihood of remaining metastases free by developing and validating a model for prediction.

This portion of task five will be begin following QNG and morphology analysis completion. We anticipate model completion by January 2001.

Research accomplishments:

- Prospective enrollment of 557 patients.
- Biochemical profile (PSA, FPSA, Complex PSA) complete on 420 patients.
- Biopsy material obtained on 493 patients.
- Histology completed on 409 cases.
- Image analysis completed on 402 cases.

Reportable outcomes:

- Manuscript in press. Reference: Steven R. Potter, M. Craig Miller, Leslie A. Mangold, Kerrie A. Jones, Jonathan I. Epstein, Robert W. Veltri, and Alan W. Partin. *Genetically Engineered Neural Networks for Predicting Prostate Cancer Progression after Radical*

Prostatectomy, Submitted June 1999.

- Poster presented at the American Urological Association Conference
  Prediction of Pathologic Stage in Clinical Stage T1c Prostate Cancer, Veltri, R.W., Miller, M.C., O'Dowd G.J., Mangold, L.A., Epstein, J.I., Partin, A.W., April 2000. (Attached)

- Abstract, Submitted to American Urological Association Confernece, April 2001
  Improved Accuracy for Prediction of Organ-Confined Prostate Cancer (Pca) in a Contemporary Referral Series: The New Challenge, Veltri, R.W., Miller, M.C., Mangold, L.A., Epstein, J.I., Sokol, L.J., and Partin, A.W. (Attached)

Appendix A

AUA 2000 ABSTRACT #839

PREDICTION OF PATHOLOGICAL STAGE IN CLINICAL STAGE TIC PROSTATE CANCERS.
Robert W. Veltri, Michael C. Miller, Gerard J. O'Dowd, Oklahoma City, OK; Leslie A. Mangold, Jonathan I. Epstein, Alan W. Partin, Baltimore, MD.

INTRODUCTION AND OBJECTIVE: A new challenge for management of prostate cancer involves the ability to predict pathologic stage in patients with clinical stage T1c disease. We constructed a statistical model to predict the organ confinement status in these patients.
METHODS: A total of 101 patients with clinical stage T1c prostate cancer were prospectively evaluated. All patients underwent radical prostatectomy at the Johns Hopkins Hospital, and the pathological staging was performed by a single pathologist (JIE). Twenty-eight percent of these patients had non-organ confined disease. Feulgen stained, 5 micron sections from the positive biopsies of these patients were reviewed and the cancer areas were graded and marked (GJO). Approximately 125 cancer nuclei were captured from the highest Gleason score area of each case utilizing an AutoCyte Pathology Workstation with QUIC-DNA vl20l software. The variance of 60 different nuclear size, shape, and chromatin texture features were calculated for each set of nuclei and used to determine a quantitative nuclear grade (QNG) for each case. The QNG, along with the patient age, highest Gleason grade (4/5), and pre-operative PSA were analyzed using logistic regression.
RESULTS: Using univariate logistic regression analysis, QNG provided the largest area under the curve (AUC 72%) compared to the other input variables, which ranged from an AUC = 58% - 63%. Applying backwards stepwise logistic regression at a stringency of $p < 0.05$ resulted in a model containing QNG, Gleason grade 4/5, and PSA with an AUC = 78% for the prediction of the disease organ confinement status. At a cutoff of 0.5, the accuracy of the model was 81%, with a positive predictive value of 74% and a negative predictive value of 83%.
CONCLUSIONS: Utilizing a new quantitative image analysis based variable, QNG, in combination with pre-operative biopsy and PSA data, we were able to more accurately predict post-operative stage in clinical stage T1c prostate cancer patients.

Source of funding: UroCor, Inc. and Department of Defense Grant #DAMD17-98-1-8468

INTRODUCTION

Prostate cancer (PCa) is the most common malignancy among men in the United States, affecting over 179,300 men and resulting in about 37,000 deaths in 1999 [1].
Approximately 30% of men who are treated for localized disease will recur, and a subset of these men will progress [2].
Prior to the commercial availability of the serum prostate specific antigen (PSA) test around 1987, the clinical staging of prostate cancer (PCa) utilized the digital rectal examination (DRE) and the transrectal ultrasound guided biopsy [2-4].
Most patients diagnosed early with organ-confined tumors are curable about 90-95% of the time with radical prostatectomy [5] or about 85-95% with radiation therapy [6].
There are a significant number (~60-70%) of patients with clinical stage T1c disease (PSA > 2.5 ng/ml and non-palpable disease) presenting at diagnosis that have advanced pathology (grade and stage) at radical prostatectomy [7-10].
Studies of various nuclear features, such as nuclear roundness and chromatin complexity, on PCa cells from radical prostatectomy sections demonstrated that nuclear morphometric descriptors (NMDs) from PCa epithelial cells are prognostic [10-11, 14].
Using computer-assisted image analysis, we applied a proprietary process to create a new pathological biomarker of genetic instability, termed Quantitative Nuclear Grade (QNG™) [10-11, 14-15] (*Figure 1*).
Using a new quantitative imaging system (*Figure 2*), we evaluated the use of the QNG™ variable in biopsy cases with Clinical Stage T1c to predict pathological stage.

MATERIALS AND METHODS

PATIENT SAMPLE

- From a total of 557 patients enrolled in a 2 ½ year prospective Prostate Cancer study funded by the Department of Defense (Grant # DAMD17-98-1-8468), we selected biopsies from a subset of men with clinical stage T1c disease where we had the following information (*Tables 1A & 1B*):
  - Age at the time of Biopsy
  - Pre-Operative PSA Level
  - Gleason Grades and Score of Biopsy
  - Feulgen Stained 5μ Tissue Section from Prostate Biopsy
  - Pathological Stage
- A total of 101 patients with clinical stage T1c underwent radical prostatectomy surgery at the Johns Hopkins Hospital, and pathological staging was performed by a single pathologist (JIE). Twenty-eight of these patients were determined to have non-organ confined disease (*Table 1A*).

QUANTATIVE NUCLEAR GRADE (QNG™) DETERMINATION:

- Feulgen stained, 5μ prostate biopsy tissue sections were reviewed and the cancer areas were graded and marked by a single pathologist (GJO).
- Approximately 125 cancer nuclei were captured from the highest Gleason score area of each case utilizing an AutoCyte Pathology Workstation with QUIC-DNA vl20l software (*Figures 1 & 2*).
- The variance of each of the 60 NMDs (i.e. different nuclear size, shape, DNA content, and chromatin texture features) were calculated for each case (*Figure 1)* [10, 11, 14, 15].
- Using univariate logistic regression analysis, the p-value and area under the receiver operator characteristics curve (ROC-AUC) for the variance of each NMD was determined (*Table 2*).
- Using backwards stepwise logistic regression at a stringency of $p < 0.20$, a multivariate model to calculate the QNG™ value was created, and it utilized 6 of the 17 univariately significant NMDs (*Table 2 & Figure 3*).

OC VS. NOC PREDICTIVE MODEL CONSTRUCTION:

- Univariate logistic regression analysis was used to determine the ability of the independent variables to predict the pathological stage (binary outcome of Organ confined [OC] vs. Non-organ confined [NOC]). (See *Table 3 & Figure 4*).
- Using the age, total PSA, presence of Gleason grade 4 and/or 5, the Gleason score, and the QNG™ value, a backwards stepwise logistic regression model was constructed with a stringency of $p < 0.05$. This multivariate model retained the total PSA, the presence of Gleason grade 4 and/or 5, and the QNG value to predict OC vs. NOC (*Table 3 & Figure 4*).

SUMMARY

- Clinical Stage T1c offers a new challenge for pre-treatment pathological staging and represents a very significant portion of prostate cancers being diagnosed today.
- Quantitative Nuclear Grade (QNG™) is an image-based morphometric measurement of genetic instability derived using a multivariately significant subset of 60 different NMDs that measure nuclear size, shape, DNA content, and chromatin organization features.
- QNG™, when combined with Gleason Grade 4/5 and total serum PSA information, predicted the pathological stage with an accuracy of 81% and a ROC-AUC of 78%.
- We plan to expand the training set to include additional biomarkers (i.e. molecular forms of PSA) and validate this clinical stage T1c pre-treatment staging algorithm.

CONCLUSIONS

- Quantitative image analysis offers a new and accurate tool to assess genetic instability cost effectively and reproducibly on both biopsy and radical prostatectomy material.
- In spite of the strong contribution of quantitative morphometry to predict the stage and progression, there remains a need to identify new and effective biomarkers that can aggregately make pre-treatment algorithms more accurate.
- Improved patient staging allows the urologist and patient to make more informed decisions for patient disease management from diagnosis through definitive treatment.

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Table 1A: Patient Sample Description (n=101 Clinical Stage T1c Prostate Cancers)

Pathologic Stage*	N	Mean Values (Median Values) tPSA (ng/ml)	Age at Biopsy	Biopsy Gleason	QNG Score
OC	73	6.1 (5.8)	57 (58)	6 (6)	0.23 (0.19)
NOC-CP	25	9.0 (6.5)	56 (56)	6 (6)	0.35 (0.28)
NOC-Mets	3	10.8 (10.6)	56 (57)	7 (7)	0.71 (0.72)

* OC = Organ Confined; NOC-CP = Non-Organ Confined due to Capsular Penetration Only; NOC-Mets = Non-Organ Confined due to Seminal Vesicle and/or Lymph Node Involvement

Table 1B:

Gleason Score	Biopsy	Radical
≤ 5	5 (5%)	6 (6%)
6	68 (67%)	79 (78%)
7	28 (28%)	14 (14%)
≥ 8	0 (0%)	2 (2%)

Figure 1: Method for QNG™ Determination

Analyze Specimen Using Image Analysis System, Generate a DNA Ploidy Histogram, and Save Nuclear Images for the Calculation of the Quantitative Nuclear Grade (QNG)

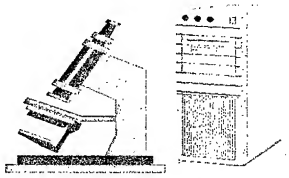
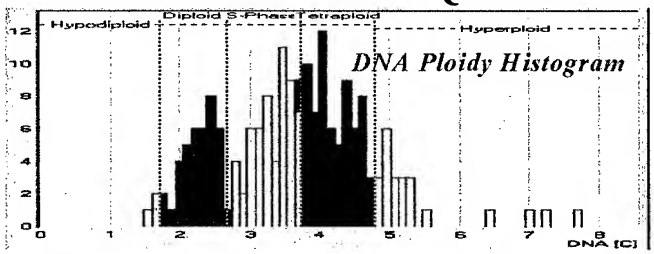
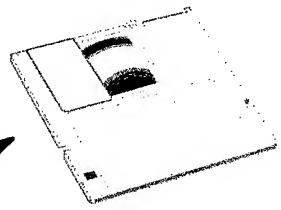


Image Analysis System



Nuclear Images



Nuclear Images saved to a Computer File

Calculate Size, Shape, and DNA complexity Features for each of the Nuclear Images saved in the Computer Files and Create the Quantitative Nuclear Grade Solution

Computer Files containing Nuclear Images

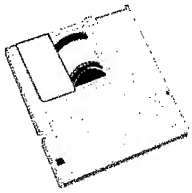
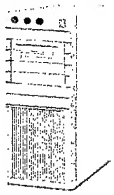
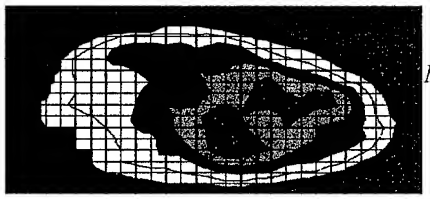


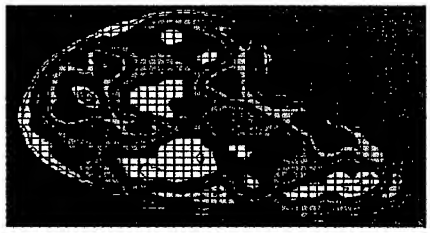
Image System Software Calculates Size, Shape, and DNA complexity Features



QNG Solution

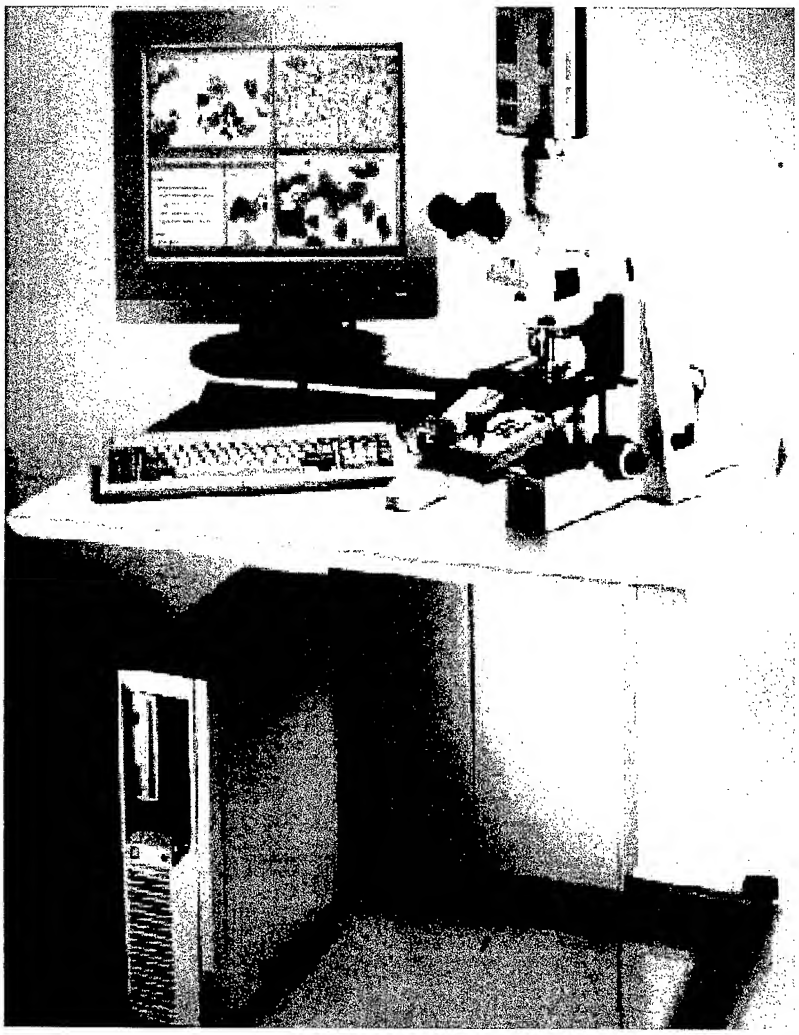


Example of Normal Prostate Cell Nuclei



Example of Non-Organ Confined Prostate Cancer Cell Nuclei

Figure 2: AutoCyte™ Pathology Workstation (TriPath Imaging Inc., Burlington, NC)



- Zeiss Axioskop Microscope
- 3CCD Color Camera
- High Resolution (768x494)
- Square Pixels
- ~60 Nuclear Morphometric Descriptors
- User Friendly Software
- High Speed / High Capacity Computer System
- Commercially Available and not Cost Prohibitive

Table 2: Logistic Regression Analysis of NMDs

AutoCyte Morphometry Measurements		Univariate Analysis OC vs. NOC Prediction	
Variable	Variable Description	p-value	ROC-AUC
Var1	Cell Class	0.0615	63.31%
Var2	Perimeter	**0.0205**	**67.27%**
Var3	Area	**0.0320**	**67.32%**
Var4	Circular Form Factor	0.8890	56.36%
Var5	*Diameter Equivalent Circle**	***0.0171***	***68.98%***
Var6	Feret X	0.0707	62.33%
Var7	Feret Y	**0.0148**	**68.93%**
Var8	Minimum Feret	**0.0413**	**66.78%**
Var9	*Maximum Feret*	***0.0181***	***67.07%***
Var10	*Area Convex Hull*	***0.0327***	***67.12%***
Var11	*Perimeter Convex Hull*	***0.0187***	***68.00%***
Var12	Excess of Gray Values	0.4589	55.33%
Var13	Skewness of Gray Values	0.2702	55.68%
Var14	StdDev of Gray Values	0.2623	57.63%
Var15	Mean Gray Value	**0.0361**	**62.57%**
Var16	Median Gray Value	**0.0405**	**61.59%**
Var17	Maximum Gray Value	0.1345	57.34%
Var18	Minimum Gray Value	0.2503	59.44%
Var19	Intensity	0.0516	65.70%
Var20	*Integrated OD*	***0.0176***	***65.66%***
Var21	Minimum OD	0.1199	57.73%
Var22	Maximum OD	0.4021	48.53%
Var23	Median OD	0.1808	57.29%
Var24	Mean OD	0.1488	57.68%
Var25	StdDev OD	0.3431	53.96%
Var26	Skewness of OD	0.4047	52.35%
Var27	Excess of OD	0.5609	48.04%
Var28	DNA Ploidy	**0.0465**	**67.07%**
Var29	DNA Index	0.1294	67.86%
Var30	Transmission	**0.0387**	**62.43%**
Var31	Variance	0.9709	52.25%
Var32	Sum Mean	0.9392	49.85%
Var33	Sum Entropy-AC	0.2730	63.26%
Var34	Sum Variance-AC	0.1345	61.99%
Var35	Cluster Shade	0.0654	62.18%
Var36	Cluster Prominence	0.0517	62.43%
Var37	Diagonal Moment	0.0759	59.20%
Var38	Kappa	0.1015	58.17%
Var39	Sum of Homogeneity	0.0533	60.23%
Var40	Angular Second Moment	**0.0159**	**65.90%**
Var41	Contrast	0.2442	56.70%
Var42	Correlation	0.5103	54.31%
Var43	Difference Moment	0.2831	55.38%
Var44	Inverse Difference Moment	0.0694	59.78%
Var45	Sum Average	0.8554	50.20%
Var46	Sum Variance-M	0.4997	55.58%
Var47	Sum Entropy-M	0.2721	59.05%
Var48	Entropy	**0.0470**	**61.59%**
Var49	Difference Variance	0.3128	55.43%
Var50	Difference Entropy	0.1220	58.32%
Var51	Information Measure A	0.1433	57.68%
Var52	Information Measure B	0.3701	61.15%
Var53	Maximal Correlation Coefficient	0.6748	51.91%
Var54	*Coefficient of Variation*	***0.0299***	***62.33%***
Var55	Peak Transition Probability	0.2280	64.73%
Var56	Diagonal Variance	**0.0159**	**65.90%**
Var57	Diagonal Moment	0.1639	60.13%
Var58	Second Diagonal Moment	0.7463	53.13%
Var59	Product Moment	0.9392	49.85%

Areas shaded in gray indicate univariately significant NMDs.

Areas shaded in yellow indicate univariately significant NMDs that were retained in the multivariate QNG model.

T1c QNG Model Predictive Index (*Xb*) Formula (*Fig. 3*):

$$Xb = -6.037824 + (Var5)(24.53941) + (Var9)(4.157673) + (Var10)(-0.0388227) + (Var11)(-2.127776) + (Var20)(0.001242) + (Var54)(5605.381)$$

$$\text{QNG Value } (P_x) = e^{Xb} / (1 + e^{Xb})$$

Table 3: Logistic Regression Analysis Results for OC vs. NOC Disease (n=101 Clinical Stage T1c PCa)

Independent Variable	p-value	ROC-AUC
Age at Biopsy	0.2501	57.53%
Pre-Operative Total PSA (ng/ml)	0.0041	61.11%
Presence of Gleason Grade 4/5	0.0113	62.94%
Gleason Score	0.0166	62.99%
QNG™	0.0001	72.31%
tPSA, Gleason Grade 4/5, QNG*	< 0.0001	77.94%

*Pred Index (*Xb*) = -3.905151 + tPSA x (0.1287485) + Gleason Grade 4/5 x (1.220584) + QNG x (5.423082) *See Figure 3 for Logistic Regression Formulas*

Figure 3: Logistic Regression Formulas

$$\text{Predicted Index } (Xb) = b_0 + b_1x_1 + \ldots\ldots + b_nx_n$$

$$\text{Pred. Probability } (P_x) = e^{Xb} / (1 + e^{Xb})$$

Where:

b_0 = Logistic regression intercept term (model constant).

b_1 - b_n = Weighting characteristic for variables x_1 - x_n.

x_1 - x_n = Independent variables used in logistic regression model.

e = natural log function

Appendix B

IMPROVED ACCURACY FOR PREDICTION OF ORGAN-CONFINED PROSTATE CANCER (PCa) IN A CONTEMPORARY REFERRAL SERIES: THE NEW CHALLENGE Veltri RW, Miller, MC, Mangold LA, Epstein JI, Sokol LJ, and Partin, AW (Presentation by Dr. Partin)

INTRODUCTION: The choice of definitive therapy for men with localized PCa is often based upon ***their*** likelihood of having organ-confined (OC) disease. This decision is currently derived from limited pre-treatment clinical and laboratory information. Nomograms such as the "Partin Tables" offer clinically useful population statistics to guide this decision process, however, do not provide patient-specific results. The changing demographics of PCa in contemporary series (e.g. PSA, Gleason Score and Clinical Stage) are unable to accurately predict pathological stage patients at this critical decision step in disease management. This study utilizes a unique combination of existing and investigational biomarkers to address this contemporary challenge in patients with T1c disease.

METHODS: We prospectively enrolled 557 men between 10/98 and 01/00 scheduled for radical prostatectomy at a single institution and 386 (69%) were diagnosed with T1c disease. Exclusion criteria included neoadjuvant treatment or medications, which could effect serologic or histologic presentation of PCa. Pre-operative sera, biopsy histology slides, clinical demographic information, prostatectomy pathology and gland weight were obtained. Biomarkers assessed included: total PSA (tPSA), complexed PSA (cPSA), freePSA (fPSA), f/tPSA ratio, Quantitative nuclear grade (QNG), cPSA-density, and biopsy Gleason score. Logistic regression was used to determine the most accurate combination of variables for predicting OC disease. A cross-validation method of data analysis was performed.

RESULTS: Complete data were available for 254/386 (66%) men with T1c disease (average age, 58.8 +/- 6 years). A total of 49/254 (19%) had pathologically non-organ-confined disease. Univariate analysis of the pre-treatment variables showed that QNG, biopsy Gleason score, tPSA, calculated f/tPSA ratio, cPSA, and cPSA density were significant. Using backward stepwise logistic regression at a stringency of $p < 0.10$, only QNG, cPSA-density, and Gleason score remained in the model and yielded an area under the ROC curve of 81.6%. The sensitivity and specificity of the model at a cutoff of 0.14 was 75.5% and 73.2% respectively with a negative predictive value of 92.6%.

CONCLUSION: These data demonstrate accurate pre-treatment prediction of OC disease in a contemporary series of men with T1c PCa based upon only use of QNG, cPSA-density and biopsy Gleason score.

DOD Study Task 1 Summary (10/25/2000)

- **Total # Patients Enrolled in Study → 557 (100%)**
- **# "Completed" Patients → 493 (89%)**
- **Total # "Completed" Patients Excluded from Study because of No Cancer on Bx or Microwave Processing → 84 (17%)**

- **Total # "Completed", Non-Excluded Patients (Cases) → 409 (83%)**
- **# "Completed", Non-Excluded Cases with Slides where Pathology Review and DNA Ploidy Analysis are Completed → 402 (98%)**
- **# "Completed", Non-Excluded Cases with Slides that need second section Feulgen stained and reviewed by Pathology → 7 (2%)**

*__Note__: *A "Completed" case refers to those where a consent form was received, a response was received from the path institution regarding the biopsy, no pre-op hormones were used, and a radical was performed.*

Appendix